

## CLAIMS

1. Method for identifying a cell-penetrating peptide or protein and/or a cell-penetrating fragment of a peptide or protein, the method comprising the steps of

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- a) obtaining the amino acid sequence of said protein or peptide,
- b) selecting the amino acid sequence of at least one candidate fragment,
- d) assessing the bulk property value  $Z_x$  of said sequence,  $Z_x$  comprising at least 5 individual average interval values  $Z_{x1}$ ;  $Z_{x2}$ ;  $Z_{x3}$ ;  $Z_{x4}$  and  $Z_{x5}$ ,

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wherein  $Z_{x1}$ ,  $Z_{x2}$ ,  $Z_{x3}$ ,  $Z_{x4}$  and  $Z_{x5}$  are average values of the respective descriptor values for the residues in said amino acid sequence, calculated with the formula

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$$Z_{\Sigma x} = (Z_{xres1} + Z_{xres2} + \dots + Z_{xresn}) / n$$

$Z_{xresy}$  being the respective descriptor value for amino acid residue y comprised in the selected candidate fragment, and wherein the descriptor value of each residue

20 corresponds to a  $Z_1$ ,  $Z_2$ ,  $Z_3$ ,  $Z_4$ , and  $Z_5$  descriptor value in a descriptor value scale as listed in **table 1A**, and

- e) identifying a cell-penetrating fragment from said at least one candidate fragment(s) based on its  $Z_x$  bulk property value,

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a cell-penetrating fragment being characterised by having a  $Z_x$  bulk property value essentially consisting of individual average interval values, wherein  $Z_{x1} < 0.2$ ;  $Z_{x2} < 1.1$ ;  $Z_{x3} < -0.49$ ;  $Z_{x4} < 0.33$ ; and  $Z_{x5} < 1.1$  and  $Z_{x5} > 0.12$ ,

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- f) optionally verifying the cell-penetrating capacity of said identified peptide or protein and/or said fragment by *in vitro* and/or *in vivo* methods.

2. Method for checking cellular penetration properties of a peptide, the method comprising

35 the steps of

- a) obtaining the amino acid sequence of the peptide,
- d) assessing the bulk property value  $Z_x$  of said sequence,  $Z_x$  comprising at least 5 individual average interval values  $Z_{x1}$ ;  $Z_{x2}$ ;  $Z_{x3}$ ;  $Z_{x4}$  and  $Z_{x5}$ ,

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wherein  $Z_{x1}$ ,  $Z_{x2}$ ,  $Z_{x3}$ ,  $Z_{x4}$  and  $Z_{x5}$  are average values of the respective descriptor values for the residues in said amino acid sequence, calculated with the formula

$$Z_{\Sigma X} = (Z_{xres1} + Z_{xres2} + \dots + Z_{xresn}) / n$$

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$Z_{xresy}$  being the respective descriptor value for amino acid residue y comprised in the selected candidate fragment, and wherein the descriptor value of each residue corresponds to a  $Z_1$ ,  $Z_2$ ,  $Z_3$ ,  $Z_4$ , and  $Z_5$  descriptor value in a descriptor value scale as listed in **table 1A**, and

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- e) checking the cell-penetrating properties of said peptide based on its  $Z_x$  bulk property value,

a cell-penetrating fragment being characterised by having a  $Z_x$  bulk property value

- 15 essentially consisting of individual average interval values, wherein  $Z_{x1} < 0.2$ ;  $Z_{x2} < 1.1$ ;  $Z_{x3} < -0.49$ ;  $Z_{x4} < 0.33$ ; and  $Z_{x5} < 1.1$  and  $Z_{x5} > 0.12$ ,

- f) synthesizing or isolating a peptide comprising the amino acid sequence of said identified cell-penetrating peptide, and  
 20 g) optionally verifying the protein-mimicking functionality and/or the cell-penetrating capacity of the synthesized or isolated peptide by *in vitro* and/or *in vivo* methods.

3. Method for producing a cell-penetrating and functional protein-mimicking peptide, the  
 25 method comprising the steps of

- a) selecting a functional protein of interest,  
 b) obtaining the amino acid sequence of said selected protein,  
 c) selecting the amino acid sequence of at least one candidate fragment  
 30 corresponding to an intracellular part of said protein,  
 d) assessing the bulk property value  $Z_x$  of said sequence,  $Z_x$  comprising at least 5 individual average interval values  $Z_{x1}$ ;  $Z_{x2}$ ;  $Z_{x3}$ ;  $Z_{x4}$  and  $Z_{x5}$ ,

- wherein  $Z_{x1}$ ,  $Z_{x2}$ ,  $Z_{x3}$ ,  $Z_{x4}$  and  $Z_{x5}$  are average values of the respective descriptor values  
 35 for the residues in said amino acid sequence, calculated with the formula

$$Z_{\Sigma X} = (Z_{xres1} + Z_{xres2} + \dots + Z_{xresn}) / n$$

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$Z_{xresy}$  being the respective descriptor value for amino acid residue y comprised in the selected candidate fragment, and wherein the descriptor value of each residue

corresponds to a  $Z_1$ ,  $Z_2$ ,  $Z_3$ ,  $Z_4$ , and  $Z_5$  descriptor value in a descriptor value scale as listed in **table 1A**, and

- 5 e) Identifying a cell-penetrating fragment from said at least one candidate fragment(s) based on its  $Z_x$  bulk property value,

a cell-penetrating fragment being characterised by having a  $Z_x$  bulk property value essentially consisting of individual average interval values, wherein  $Z_{x1} < 0.2$ ;  $Z_{x2} < 1.1$ ;  $Z_{x3} < -0.49$ ;  $Z_{x4} < 0.33$ ; and  $Z_{x5} < 1.1$  and  $Z_{x5} > 0.12$ ,

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- f) synthesizing or isolating a peptide comprising the amino acid sequence of said identified cell-penetrating peptide, and  
g) optionally verifying the protein-mimicking functionality and/or the cell-penetrating capacity of the synthesized or isolated peptide by *in vitro* and/or *in vivo* methods.

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4. Method for *de novo* designing and producing an artificial cell-penetrating and/or an artificial cell-penetrating and functional protein-mimicking peptide, the method comprising  
20 the steps of

- a) designing at least one artificial peptide and/or peptide fragment,  
d) assessing the bulk property value  $Z_x$  of the amino acid sequence of said artificial peptide or peptide fragment,  $Z_x$  comprising at least 5 individual  
25 average interval values  $Z_{x1}$ ;  $Z_{x2}$ ;  $Z_{x3}$ ;  $Z_{x4}$  and  $Z_{x5}$ ,

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wherein  $Z_{x1}$ ,  $Z_{x2}$ ,  $Z_{x3}$ ,  $Z_{x4}$  and  $Z_{x5}$  are average values of the respective descriptor values for the residues in said amino acid sequence, calculated with the formula

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$$Z_{\Sigma x} = (Z_{xres1} + Z_{xres2} + \dots + Z_{xresn}) / n$$

- $Z_{xresy}$  being the respective descriptor value for amino acid residue y comprised in the  
35 selected candidate fragment, and wherein the descriptor value of each residue corresponds to a  $Z_1$ ,  $Z_2$ ,  $Z_3$ ,  $Z_4$ , and  $Z_5$  descriptor value in a descriptor value scale as listed in **table 1A**, and

- 40 e) checking the cell-penetrating properties of said artificial peptide and/or peptide fragment based on its  $Z_x$  bulk property value,

a cell-penetrating fragment being characterised by having a  $Z_x$  bulk property value essentially consisting of individual average interval values, wherein  $Z_{x1} < 0.2$ ;  $Z_{x2} < 1.1$ ;  $Z_{x3} < -0.49$ ;  $Z_{x4} < 0.33$ ; and  $Z_{x5} < 1.1$  and  $Z_{x5} > 0.12$ ,

f) synthesizing said peptide and/or peptide fragment comprising the amino acid sequence identified as cell penetrating, and

5 g) optionally verifying the protein-mimicking functionality and/or the cell-penetrating capacity of the synthesized peptide and/or peptide fragment by *in vitro* and/or *in vivo* methods.

10 5. Method according to any of claims 1-4, wherein said amino acid sequence after step e) is additionally

h) assessed and selected for having a property value essentially consisting of individual average interval values, wherein  $Z_{\Sigma Bulkha} > 3.1$  and  $Z_{\Sigma Bulkha} < 8.13$  and  $Z_{\Sigma 1} > -1.25$  and  $Z_{\Sigma 1} < 3.52$  and  $Z_{\Sigma 2} > -3.9$  and  $Z_{\Sigma 2} < 3.1$  and  $Z_{\Sigma 3} < -0.5$  and  $Z_{\Sigma 3} > -3.51$  and  $Z_{\Sigma hdb} > -0.115$  and  $Z_{\Sigma hdb} < 5.1$  and  $hdb > 0$  and  $hdb < 84$ .

6. Method according to any of claims 1-4, wherein said amino acid sequence after step e) is additionally

20 h) assessed and selected for having a property value essentially consisting of individual average interval values, wherein  $Z_{\Sigma Bulkha} > 3.2$  and  $Z_{\Sigma Bulkha} < 5.9$  and  $Z_{\Sigma 1} > -1.25$  and  $Z_{\Sigma 1} < 1.92$  and  $Z_{\Sigma 2} > -1.22$  and  $Z_{\Sigma 2} < 1.29$  and  $Z_{\Sigma 3} < -0.5$  and  $Z_{\Sigma 3} > -1.94$  and  $Z_{\Sigma hdb} > 0.28$  and  $Z_{\Sigma hdb} < 2$  and  $hdb > 5$  and  $hdb < 30$ .

25 7. Method according to any of claims 1-4, wherein said amino acid sequence after step e) is additionally

30 h) assessed and selected for having a property value essentially consisting of individual average interval values, wherein  $Z_{\Sigma Bulkha} > 3.2$  and  $Z_{\Sigma Bulkha} < 4.8$  and  $Z_{\Sigma 1} > -1.1$  and  $Z_{\Sigma 1} < 1.92$  and  $Z_{\Sigma 2} > -1.1$  and  $Z_{\Sigma 2} < 0$  and  $Z_{\Sigma 3} < -0.55$  and  $Z_{\Sigma 3} > -1.94$  and  $Z_{\Sigma hdb} > -0.28$  and  $Z_{\Sigma hdb} < 1.57$  and  $hdb > 7$  and  $hdb < 25$ .

8. Method according to any of claims 1-4, wherein steps d) and e) are exchanged for

35 h) assessing and selecting an amino acid sequence for having a property value essentially consisting of individual average interval values, wherein  $Z_{\Sigma Bulkha} > 3.1$  and  $Z_{\Sigma Bulkha} < 8.13$  and  $Z_{\Sigma 1} > -1.25$  and  $Z_{\Sigma 1} < 3.52$  and  $Z_{\Sigma 2} > -3.9$  and  $Z_{\Sigma 2} < 3.1$  and  $Z_{\Sigma 3} < -0.5$  and  $Z_{\Sigma 3} > -3.51$  and  $Z_{\Sigma hdb} > -0.115$  and  $Z_{\Sigma hdb} < 5.1$  and  $hdb > 0$  and  $hdb < 84$ .

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9. Method according to any of claims 1-4, wherein steps d) and e) are exchanged for

h) assessing and selecting an amino acid sequence for having a property value essentially consisting of individual average interval values, wherein  $Z_{\Sigma Bulkha}$

$> 3.2$  and  $Z_{\Sigma Bulkha} < 5.9$  and  $Z_{\Sigma 1} > -1.25$  and  $Z_{\Sigma 1} < 1.92$  and  $Z_{\Sigma 2} > -1.22$  and  $Z_{\Sigma 2} < 1.29$  and  $Z_{\Sigma 3} < -0.5$  and  $Z_{\Sigma 3} > -1.94$  and  $Z_{\Sigma hdb} > 0.28$  and  $Z_{\Sigma hdb} < 2$  and  $hdb > 5$  and  $hdb < 30$ .

5 10. Method according to any of claims 1-4, wherein steps d) and e) are exchanged for

h) assessing and selecting an amino acid sequence for having a property value essentially consisting of individual average interval values, wherein  $Z_{\Sigma Bulkha} > 3.2$  and  $Z_{\Sigma Bulkha} < 4.8$  and  $Z_{\Sigma 1} > -1.1$  and  $Z_{\Sigma 1} < 1.92$  and  $Z_{\Sigma 2} > -1.1$  and  $Z_{\Sigma 2} < 0$  and  $Z_{\Sigma 3} < -0.55$  and  $Z_{\Sigma 3} > -1.94$  and  $Z_{\Sigma hdb} > -0.28$  and  $Z_{\Sigma hdb} < 1.57$  and  $hdb > 7$  and  $hdb < 25$ .

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11. A method according to any of claims 1 to 10, wherein said protein is a transmembranal protein.

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12. A method according to claim 11, wherein said protein is a protein selected from the group consisting of human PrpC, bovine PrpC, amyloid precursor protein (APP) and presenilin-1 (PS-1).

20 13. A method according to claim 11, wherein said protein is a mammalian receptor, such as a receptor belonging to the superfamily of tyrosine kinase receptors, a 7TM receptor and/or a G-protein coupled receptor.

14. A method according to claim 13, wherein said protein is a protein selected from the group consisting of the GLP-1 receptor, AT1A receptor, and Dopamine-2 receptor.

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15. A method according to any of the preceding claims, wherein the cell-penetrating capacity of said peptide and/or peptide fragment is verified by monitoring the cellular uptake rate of a detectable dye into said cell after exposure to said peptide and/or peptide fragment.

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16. A method according to claim 15, wherein said dye is fluorescein.

17. A cell-penetrating peptide and/or a non-peptide analogue thereof obtained by a method according to any of the preceding claims.

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18. A cell-penetrating peptide essentially consisting of a peptide obtained by a method according to any of the preceding claims.

40 19. A cell-penetrating peptide selected from a 8 to 50 amino acid residues long peptide, or a fragment thereof with cell-penetrating capacity.

20. A cell-penetrating peptide according to claim 19, wherein the peptide is 14 to 30 amino acid residues long.

21. A cell-penetrating peptide according to claim 19, wherein the peptide is 16 to 20 amino acid residues long.

5 22. A cell-penetrating peptide selected from a 8 amino acid residues long peptide or a fragment of a peptide corresponding to one of the amino acid sequences listed in SEQ.ID.NO. 6234-7420.

10 23. A cell-penetrating peptide selected from a 12 to 50 amino acid residues long peptide or a fragment of a peptide corresponding to one of the amino acid sequences listed in SEQ.ID.NO. 1-150.

15 24. A cell-penetrating peptide selected from a 12 amino acid residues long peptide or a fragment of a peptide corresponding to one of the amino acid sequences listed in SEQ.ID.NO. 151-2684.

20 25. A cell-penetrating peptide selected from a 12 amino acid residues long peptide or a fragment of a peptide corresponding to one of the amino acid sequences listed in SEQ.ID.NO. 7421-11649.

26. A cell-penetrating peptide selected from a 16 amino acid residues long peptide or a fragment of a peptide corresponding to one of the amino acid sequences listed in SEQ.ID.NO. 2685-6233.

25 27. A cell-penetrating peptide selected from a 16 amino acid residues long peptide or a fragment of a peptide corresponding to one of the amino acid sequences listed in SEQ.ID.NO. 11650-18398.

30 28. A cell-penetrating functional protein-mimicking peptide that is derived from a transcription factor or designed to closely resemble a transcription factor or at least a functional fragment of a transcription factor.

35 29. A cell-penetrating peptide selected from a 8-16 amino acid residues long peptide or a fragment of a peptide corresponding to one of the amino acid sequences listed in SEQ.ID.NO. 18399-31839.

30. A cell-penetrating functional protein-mimicking peptide that is derived from a secretase or designed to closely resemble a secretase or at least a functional fragment of a secretase.

40 31. A cell-penetrating peptide selected from a peptide or a fragment of a peptide corresponding to one of the amino acid sequences listed in SEQ.ID.NO. 31840-31864.

32. A cell-penetrating functional protein-mimicking peptide that is derived from a GLP-1 receptor or designed to closely resemble a GLP-1 receptor or at least a functional fragment of a GLP-1 receptor.
- 5 33. A cell-penetrating peptide selected from a peptide or a fragment of a peptide corresponding to one of the amino acid sequences listed in SEQ.ID.NO. 31865-31886.
34. A cell-penetrating functional protein-mimicking peptide that is derived from a CGRP receptor or designed to closely resemble a CGRP receptor or at least a functional fragment
- 10 of a CGRP receptor.
35. A cell-penetrating peptide selected from a peptide or a fragment of a peptide corresponding to the amino acid sequence listed in SEQ.ID.NO. 31895.
- 15 36. A cell-penetrating functional protein-mimicking peptide that is derived from an AT2 type receptor or designed to closely resemble an AT2 type receptor or at least a functional fragment of an AT2 type receptor.
37. A cell-penetrating peptide selected from a peptide or a fragment of a peptide
- 20 corresponding to one of the amino acid sequences listed in SEQ.ID.NO. 31887-31894.
38. A cell-penetrating functional protein-mimicking peptide that is derived from a PrpC or designed to closely resemble a PrpC or at least a functional fragment of a PrpC.
- 25 39. A cell-penetrating peptide selected from a peptide or a fragment of a peptide corresponding to one of the amino acid sequences listed in SEQ.ID.NO. 31896-31899.
40. A cell-penetrating functional protein-mimicking peptide that is derived from amyloid precursor protein (APP) or presenilin-1 (PS-1) or designed to closely resemble amyloid
- 30 precursor protein (APP) or presenilin-1 (PS-1) or at least a functional fragment of amyloid precursor protein (APP) or presenilin-1 (PS-1).
41. A cell-penetrating peptide selected from a peptide or a fragment of a peptide corresponding to one of the amino acid sequences listed in SEQ.ID.NO. 31900-31906.
- 35 42. A functional analogue of a cell-penetrating peptide according to any of claims 19 to 41.
43. A cell-penetrating peptide and/or a non-peptide analogue thereof being at least 75% identical to a cell-penetrating peptide and/or a non-peptide analogue thereof according to
- 40 any of claims 19 to 41.
44. A cell-penetrating peptide and/or a non-peptide analogue thereof comprising a cell-penetrating peptide and/or a non-peptide analogue thereof according to any of claims 19 to 41.

45. A cell-penetrating peptide and/or a non-peptide analogue thereof according to any of claims 19 to 44, selected from the group consisting of peptides comprising the amino acid sequence IVIAKLKA and/or a cell membrane penetrating functional analogue thereof.

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46. A cell-penetrating peptide and/or a non-peptide analogue thereof according to claim 45, comprising the amino acid sequence IVIAKLANLMCKTCRLAK.

47. A cell-penetrating peptide and/or a non-peptide analogue thereof according to any of claims 19 to 46, wherein the peptide is coupled to a cargo.

48. A cell-penetrating peptide and/or a non-peptide analogue thereof according to claim 47, wherein the peptide is coupled to a cargo by a S-S bridge.

49. A cell-penetrating peptide and/or a non-peptide analogue thereof according to claim 47 or 48, wherein the cargo is a cellular effector.

50. A cell-penetrating peptide and/or a non-peptide analogue thereof according to any of claims 47 to 49, wherein the cargo is a pharmaceutically active component.

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51. A cell-penetrating peptide and/or a non-peptide analogue thereof according to any of claims 47 to 50, wherein the cargo is selected from the group consisting of a small molecule, peptide, protein, saccharide, single and/or double stranded oligonucleotide, plasmid, antibiotic substance, cytotoxic and/or antiviral agent.

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52. A cell-penetrating peptide and/or a non-peptide analogue thereof according to any of claims 47 to 51, wherein the cargo is a marker molecule.

53. A cell-penetrating peptide and/or a non-peptide analogue thereof according to any of claims 47 to 51, selected from a peptide or a fragment of a peptide corresponding to one of the amino acid sequences listed in SEQ.ID.NO. 31907-31922.

54. A cell-selective delivery system for a cytostatic and/or cytotoxic agent, comprising  
a) a cell-penetrating peptide and/or a non-peptide analogue thereof  
comprising a protease consensus site for a protease specifically  
overexpressed in and/or secreted by a target cell and

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b) a cytostatic and/or cytotoxic agent,

wherein said cell-selective delivery system additionally comprises an inactivation sequence repressing the activity of said cell-penetrating peptide, and which is cleaved by said  
protease upon introducing said cell-selective delivery system in the near vicinity of said  
target cell.

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55. A vector for transfecting a cell, the vector comprising  
a) a nucleic acid component,



b) a polycation conjugate, and

c) a cell-penetrating peptide and/or a non-peptide analogue thereof,

wherein the average rate of transfection per cell at identical transfection conditions is enhanced by a factor of at least 2, compared to a vector comprising only components a)

5 and b), or only components a) and c).

56. A vector according to claim 55, wherein said vector is used in a transient transfection and/or a stable transfection of a cell.

10 57. A vector according to claim 56, wherein said vector is used in an *in vivo* and/or in an *in vitro* transfection of a cell.

58. A vector according to claim 57, wherein said vector is used for a non-viral transfection of a cell.

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59. A vector according to any of claims 55-58, wherein said polycation conjugate is polyethylene imine (PEI).

60. A vector according to any of claims 55-59, selected from a peptide or a fragment of a  
20 peptide corresponding to the amino acid sequence listed in SEQ.ID.NO. 31913.

61. A vector according to any of claims 55-59, wherein said cell-penetrating peptide is a peptide or a peptide fragment according to any of claims 22-27, 29, 31, 33, 35, 37, 39, 41, 45, 46, 52 and 60.

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62. A cell-penetrating peptide and/or a non-peptide analogue thereof and/or a vector according to any of claims 22-27, 29, 31, 33, 35, 37, 39, 41, 45, 46, 52, 59 and 55-60, further characterised by being cell and/or cell-type and/or tissue specific.

30 63. A cell-penetrating peptide and/or a non-peptide analogue thereof and/or a vector according to claim 62, wherein said peptide and/or a non-peptide analogue thereof and/or vector selectively interacts with a cell surface protein, thus mediating the cell and/or cell-type and/or tissue specific cellular penetration.

35 64. A cell-penetrating peptide and/or a non-peptide analogue thereof and/or a vector according to claim 63, wherein said cell surface protein is over-expressed in said specific cell and/or cell-type and/or tissue.

65. A cell-penetrating peptide and/or a non-peptide analogue thereof and/or a vector  
40 according to claim 63 or 64, wherein said cell surface protein is selected from the group consisting of receptor tyrosine kinase type receptors, glycosphingolipids, CD44, erbB2, erbB3, and neuropeptide receptors.

66. A cell-penetrating peptide and/or a non-peptide analogue thereof and/or a vector according to claim 62, wherein said peptide and/or vector selectively interacts with an over-expressed cellular and/or extracellular protein, thus mediating the cell and/or cell-type and/or tissue specific cellular penetration.

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67. A cell-penetrating peptide and/or a non-peptide analogue thereof and/or a vector according to claim 62, wherein said over-expressed protein is selected from the group consisting of agonists and antagonists to cell and/or cell-type and/or tissue specific receptors.

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68. A cell-penetrating peptide and/or a non-peptide analogue thereof and/or a vector according to claim 62 or 63, wherein said over-expressed protein is selected from the group consisting of proteases, protease inhibitors and protease activators.

15 69. Use of a cell-penetrating peptide and/or a non-peptide analogue thereof and/or a vector according to any of claims 17-68 and/or a cell-selective delivery system according to claim 54 for the manufacture of a pharmaceutical composition.

70. A pharmaceutical composition manufactured according to claim 69.

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71. Use of a cell-penetrating peptide and/or a non-peptide analogue thereof and/or a vector and/or a cell-selective delivery system and/or a pharmaceutical composition according to any of claims 17-68 for gene therapy.

25 72. Use of a cell-penetrating peptide and/or a non-peptide analogue thereof and/or a vector and/or a cell-selective delivery system according to any of claims 17-68 for the manufacture of a pharmaceutical composition for gene therapy.

30 73. Use of a cell-penetrating peptide and/or a non-peptide analogue thereof and/or a vector and/or a cell-selective delivery system according to any of claims 17-68 for the manufacture of a drug delivery system for transmembrane transport across an epithelial membrane, such as across the epithelium in the intestinal/buccal system, the mucosa in the mouth, lung, rectum or nose, or the blood brain barrier of a mammal.

35 74. Use of a cell-penetrating peptide and/or a non-peptide analogue thereof and/or a vector, a pharmaceutical composition and/or a drug delivery system according to any of claims 17-68 for the manufacture of a pharmaceutical composition for treating and/or preventing a medical condition selected from the group consisting of infectious diseases, diabetes type I, diabetes type II, Alzheimers Disease, Parkinsons Disease, cancer.

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75. Method for treating a patient who suffers from a medical condition, the method comprising administering a pharmaceutical composition comprising a cell-penetrating peptide and/or a non-peptide analogue thereof and/or a vector, a pharmaceutical

composition and/or a drug delivery system according to any of claims 17-68 to a patient in need thereof.

76. Method of treating a patient who suffers from a medical condition selected from the group consisting of diabetes type I and II, Alzheimers Disease, Parkinsons Disease, a prion disease, a cardiovascular disease, an infectious disease, disorders resulting from perturbed signal transduction, or cancer, the method comprising administering a pharmaceutical composition comprising a cell-penetrating peptide and/or a non-peptide analogue thereof and/or a vector, a pharmaceutical composition and/or a drug delivery system according to any of claims 17-68 is administered to a patient in need thereof.